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REMARKS

Present Status of the Application

The Office maintains its rejection to claims 1-8, 10-13 and 15 under 35 U.S.C. 102(b), as being anticipated by Bellhouse et al. (WO/94/24263) and to claims 1-15 under 35 U.S.C. 103(a) as being unpatentable over Bellhouse et al. (WO 94/24263, hereinafter Bellhouse) in view of Bhat et al. (J. Appl. Genet. 2001, 42(4) : 405-412, hereinafter Bhat).

Applicants have amended claims 1 and 11 to more clearly define the present invention. Supports for the amendments to the claims are described at paragraphs [0028]-[0029], [0034]-[0034], [0045], [0049]-[0052] and Figure 1 of the specification. It is believed that no new matter is added by way of these amendments made to the claims or otherwise to the application. After entry of the foregoing amendments, claims 1-15 remain pending in the present application.

Applicants have most respectfully considered the remarks set forth in this Office Action. Regarding the anticipation and obvious rejections, it is however strongly believed that the cited references are deficient to adequately teach the claimed features as recited in the presently pending claims. The reasons that motivate the above position of the Applicants are discussed in detail hereafter, upon which reconsideration of the claims is most earnestly solicited.

Rejection under 35 U.S.C 102 (b)

Applicants respectfully traverse the 102(b) rejection of claims 1-8, 10-13 and 15 because Bellhouse et al. (WO/94/24263) does not teach every element recited in these claims.

> In order to properly anticipate Applicants' claimed invention under 35 U.S.C 102, each and every element of claim in issue must be found, "either expressly or inherently described, in a single prior art reference". "The identical invention must be shown in as complete details as is contained in the .... claim. Richardson v. Suzuki Motor Co., 868 F. 2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)." See M.P.E.P. 2131, 8th ed., 2001.

The present invention is in general related a method of delivering a biological material **in a liquid state free of metal particles** using a gene gun and a method for gene transformation by using a gene gun respectively as claims 1 and 10 recite:

Claim 1. A method for delivering a biological material using a gene gun, comprising:

providing the gene gun comprising a pressurized chamber, a sprayer, a controller valve and a material delivery system;

placing a **sample solution free of metal particles** into the material delivery system, wherein the sample solution comprises at least the biological material;

triggering the gene gun and providing a gas through the controller valve to the pressurized chamber until the gas establishes a pressure lower than 4 atm;

releasing the liquid sample solution from the material delivery system, so that the sample solution is accelerated by the gas in the pressurized chamber; and

discharging the sample solution out of the sprayer, wherein the sprayer includes a spray nozzle and a spray tube, and the spray nozzle comprises an interior contour, wherein the interior contour of the spray nozzle comprises a diverging part and a converging part and a spray neck positioned between the diverging part and the converging part, wherein **the sample solution is released from the material delivery system around the spray neck of the spray nozzle and is released in a direction perpendicular to a direction of the flow of the gas**, and the spray tube is a diverging straight tube, so that a discharge speed of the sample solution is supersonic and the biological material is evenly injected into a target.

Claim 11. (currently amended) A method for gene transformation by using a gene gun, comprising:

providing the gene gun comprising a pressurized chamber, a sprayer, a controller valve and a material delivery system;

placing a **sample solution free of metal particles** into the material delivery system, wherein the sample solution comprises at least a nucleic acid;

triggering the gene gun and providing a gas through the controller valve to the pressurized chamber to establish a pressure lower than 4 atm, wherein the gas is a nitrogen gas or a helium gas;

releasing the liquid sample solution from the material delivery system after the gas in the pressurized chamber establishes the pressure, so that the sample solution is accelerated by the gas in the pressurized chamber; and

discharging the liquid sample solution out of the sprayer, wherein the sprayer includes a spray nozzle and a spray tube, and the spray nozzle comprises an interior contour, wherein the interior contour of the spray nozzle comprises a diverging part and a converging part and **a spray neck positioned between the diverging part and the converging part, wherein the liquid sample solution is released from the material delivery system around the spray neck of the spray nozzle and is released in a direction perpendicular to a direction of the flow of the gas**, and the spray tube is a diverging straight tube, so that a discharge speed of the liquid sample solution is supersonic and the biological material is evenly injected into a target.

Applicants respectfully submit Bellhouse fails to disclose, teach or suggest the sample used in the delivery system is a liquid sample solution free of metal particles, and the liquid sample solution is released from the material delivery system around the spray neck of the spray nozzle and the liquid sample solution is released in a direction perpendicular to a direction of the flow of the gas; and thus, Bellhouse does not teach each and every element in claims 1 and 11.

Bellhouse basically discloses a system used for a ***delivery of solid particles***. More specifically, Bellhouse teaches, on page 4, lines 34-37, the delivery of **dry powdered** therapeutic agent. Bellhouse explicitly teaches away the delivery of a liquid sample since "a particular

advantage of the new technique of injecting dry powdered drugs is that it can be used for delivering a stable mixture of drugs, which are unstable when mixed wet".

As taught in claims 1 and 11, the present invention is directed to a delivery of a sample solution that is in a liquid state. The present invention specifically teaches a gene gun system which is able to deliver a liquid sample solution to a target at high speed and low pressure. It is particular important that the liquid sample solution of the instant case is free of solid particles, such as metal carriers, to obviate problems of cells deaths that are often occurred in a particle gun system. Applicants respectfully disagree with the Examiner's assertion that the powdery particles of Bellhouse can be construed as a "solution". The definition of "solution" in chemistry is a "**homogenous mixture** of two or more substances in relative amounts that can be varied continuously up to what is called the limit of solubility. The term **solution** is commonly applied to **the liquid state** of matter, but solutions of gases and solids are possible. Air, for example, is a solution consisting chiefly of oxygen and nitrogen with trace amount..., wherein **a solid solution refers to an alloy**..." (cited from Encyclopedia Britannica). Bellhouse teaches solid particles of powdered therapeutic agent. By definition, powder is "any mass of **fine particles** or dust prepared by various mechanical means, e.g. **grinding of solid substances**, or by chemical means, e.g. **precipitation from solutions**. In a special sense, the word is applied to powdered propellant explosives, e.g. gunpowder, and to powdered substances that produce a bright light when ignited." (Http://www.answers.com/topic/powder). In brief, a powdered therapeutic agent is substantially different from a solution of the instant case. In a similar token, Bhat teaches that a sample is a suspension which is a mixture containing gold particles in water, and the gold

particles **are not homogenously mixed** in water. In fact, gold powders and water are easily separated into two phases (a solid phase and a liquid phase). Therefore, the sample of Bhat can not be construed as a "solution". Accordingly, both Bellhouse and Bhat at least fails to teach or suggest the claimed invention in this regard.

The present invention further teaches that the liquid sample solution is released from the material delivery system around the spray neck of the spray nozzle and is released in a direction perpendicular to a direction of the flow of the gas. As clearly demonstrated in Figure 1 and described in paragraph [0028] of the specification, the material delivery system 108 is configured around the spray neck of the spray nozzle 104b, between the converging part and the diverging part. The droplets of the liquid sample solution are then released from the material delivery system into the spray nozzle at the spray neck region. Additionally, the droplets of the liquid sample solution are released from the material delivery system in a direction perpendicular to the direction of the gas flow, and the sample solution is then accelerated by the gas in the spray nozzle. Bellhouse, on the other hand, teaches the capsule 28, which comprises the compartment 32 containing particles to be injected, being positioned between the pressure chamber 25 and the upper convergent part 35 of the nozzle, while the convergent part 35 of the nozzle 26 further leads through a throat 36 to a divergent part 37 (Please refer to page 17, lines 13-34, page 18, 3-5, Figure 1). The powdered sample of Bellhouse is released from the compartment 32 to the upper converging part 35 of the nozzle 26 as the gas travel from the pressure chamber 25 through the compartment 32. In other words, the powdered sample is released from the compartment 32 in a direction that is along the direction of the gas flow. The gas with the powdered sample entrained

thereby is then traveled through the throat 36 to the divergent part 37 of the nozzle 26. Accordingly, Bellhouse fails to teach releasing a liquid sample solution from the material delivery system around the spray neck of the spray nozzle and releasing a liquid sample in a direction perpendicular to a direction of the flow of the gas.

Moreover, Bellhouse teaches that "the divergent portion is 50 mm long and the diameters at 5 mm increments from the throat 36 downstream to the outlet end of the nozzle are 1.74, 1.95, 2.03, 2.10, 2.16, 2.19, 2.20, 2.21, 2.22 and 2.23 mm respectively". Applicants submit that the divergent portion 37 is not linearly diverged from the throat 36 to the outlet end of the nozzle because the slope of these sections of the divergent portion varies from 5 mm to the outlet end of the nozzle. However, the diverging part of the present invention linearly diverges to the outlet end of the spray as recited in claims 1 and 11.

For at least the foregoing reasons, Applicants respectfully submit that independent claims 1 and 11 patently define over the prior art reference, and should be allowed. For at least the same reasons, dependent claims 2-10 and 12-15 patently define over the prior art as a matter of law, for at least the reason that these dependent claims contain all features of their respective independent claim.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellhouse in view of Bhat et al. (J. Appl. Genet. 2001, 42(4):405-412, hereinafter Bhat).

With regard to the rejections of claims 1-15 by Bellhouse in view of Bhat, Applicants respectfully submit that these claims patently define over the prior art for at least the same reasons discussed above.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Further, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Bhat is directed to a gene transfer method using a standard particle inflow gun (PIG) with gold particles as carrier of biological materials. In Bhat, the particle inflow gun uses a pressure of 2-6 barr. In essence, the operation method of the device disclosed in Bhat is different from the present application because the operation method of Bhat is operated in a vacuum condition (28 mm-Hg, shown in Table 1), while the method of the present invention is not operated in a vacuum condition (as claimed in claims 8 & 13) but at 1 atmospheric pressure. In summary, the acceleration theory of the particle inflow gun is different from that of the instant case, and thus the design of the apparatus and the method of using the apparatus are significantly different. Further, as previously discussed, Bhat teaches a mixture containing gold particles in which the gold particles **are not homogenously mixed** in water, and Bellhouses teaches a dry powdered sample. Accordingly, independent claims 1 and 11 of the present invention is non-obvious over Bellhouse in view of Bhat because the combination of Bellhouse and Bhat at least fails to teach (1) a sample solution which is a homogeneous mixture in a liquid state and is free of metal particles (2) a sample solution being released from the material delivery system around the spray

neck of the spray nozzle and being released in a direction perpendicular to a direction of the flow of the gas.

Additionally, prima facie obviousness has not been established at least because the requisite motivation to combine Bellhouse in view of Bhat is lacking. Applicant submits that there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. First of all, Bellhouse teaches away a wet sample; therefore, there is no suggestion from Bellhouse to modify Bellhouse' system for dry powdered sample to a system for liquid sample solution. Second, the devices used in Bellhouse and Bhat are very different devices. Bhat teaches a system for a suspension of gold particles, while Bellhouses teaches a system for powdered particles.

Further, the determinations of obviousness must be supported by evidence in the record. See In re Zurko, 258 F.3d 1379, 1386 (Fed. Cir. 2001) (finding that the factual determinations central to the issue of patentability, including conclusions of obviousness by the Board, must be supported by "substantial evidence"). Applicants respectfully disagree with the Office's contention that the interior contour of the converging part of the spray neck at the section labeled 35 of Bellhouse appears to meet the limitation of claims 9 and 14 defined by the range rt<Rt,2rt". Applicants respectfully submit that the Office has failed to provide substantial evidence that is a result of a thorough factual inquiry; instead, the obvious determination is based on unsubstantiated presumption.

For at least these reasons, Applicants respectfully submit that claims 1 and 11 of the invention are in condition of allowance. Since claims 2-10 and 12-15 are dependent claims, which further define the invention recited in claims 1 & 11, respectively, Applicants respectfully assert that these claims are also in condition for allowance. Reconsideration and withdrawal of the rejections are thereby courteously requested.

CONCLUSION

For at least the foregoing reasons, it is believed that the pending claims are in proper condition for allowance. If the Examiner believes that a telephone conference would expedite the examination of the above-identified patent application, the Examiner is invited to call the undersigned.

Respectfully submitted,
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Date: 3/19/2007

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